VOS-22

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner	:	Not yet assigned
Group	:	1645
Applicants	:	Christian Plank et al.
Application No.	:	10/023,317 Confirmation No. : 2272
Filed	:	December 17, 2001
For	:	COMBINATIONS FOR INTRODUCING NUCLEIC ACIDS INTO CELLS

New York, New York
March 28, 2002

Hon. Commissioner for Patents
P.O. Box 2327
Arlington, VA 22202

SUPPLEMENTAL PRELIMINARY AMENDMENT

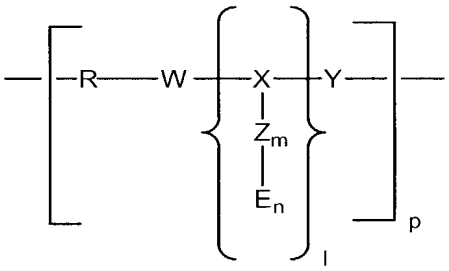
Sir:

Prior to the issuance of the first Office Action in the above-identified application, kindly amend the application as follows:

IN THE SPECIFICATION

Replace the paragraph from page 4, line 4 to page 6, line 1 with the following:

The present invention relates in its first aspect to a charged copolymer having the general formula I

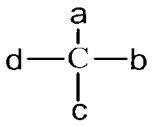


wherein R is an amphiphilic polymer or a homo- or hetero-bifunctional derivative thereof,

and wherein X

i) is an amino acid or an amino acid derivative, a peptide or a peptide derivative or a spermine or a spermidine derivative; or

ii) wherein X is



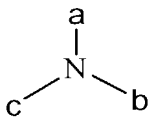
wherein

a is H or, optionally halogen- or dialkylamino-substituted, C_1-C_6 alkyl;

and wherein

b, c and d are the same or different, optionally halogen- or dialkylamino-substituted, C_1-C_6 alkylene; or

iii) wherein X is



wherein

a is H or, optionally halogen- or dialkylamino-substituted, C_1-C_6 alkyl,

and wherein

b and c are the same or different, optionally halogen- or dialkylamino-substituted, C_1-C_6 alkylene; or

iv) wherein X

is a substituted aromatic compound with three functional groupings $W_1Y_1Z_1$, wherein W, Y and Z have the meanings mentioned below;

wherein

W, Y or Z are the same or different groups CO, NH, O or S or a linker grouping capable of reacting with SH, OH, NH or NH_2;

and wherein the effector molecule E
is a cationic or anionic peptide or peptide derivative or a spermine or spermidine derivative or a glycosaminoglycane or a non-peptidic oligo/polycation or -anion; wherein
m and n are independently of each other 0, 1 or 2; wherein

p preferably is 3 to 20; and wherein

l is 1 to 5, preferably 1.
If l is > 1, the moiety $X\text{-}Z_m\text{-}E_n$ is the same or different.

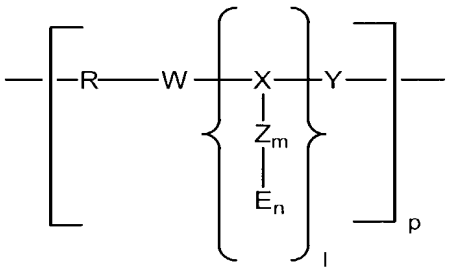
Replace the priority claim on page 1, on the first line of the application after the title with the following:

This application claims benefit under 35 U.S.C. §§ 120 and 365(c) from International Application No. PCT/EP00/05778, filed June 21, 2000, which was published in the German language.

IN THE CLAIMS

Replace claims 1, 5-9 and 12-14 with substitute claims 1, 5-9 and 12-14 as follows:*

1. (Twice Amended) A combination of a carrier and a complex comprising a nucleic acid molecule and a charged copolymer of the general formula I

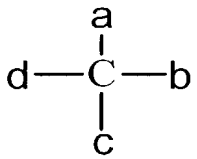


wherein R is an amphiphilic polymer or a homo- or hetero-bifunctional derivative thereof,

and wherein X

i) is an amino acid or an amino acid derivative, a peptide or a peptide derivative or a spermine or a spermidine derivative; or

ii) wherein X is



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* Applicants enclose a "Version Showing Changes Made" including the amendments to the specification and to the claims.

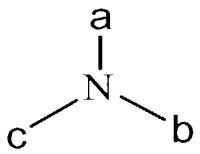
wherein

a is H or, optionally halogen- or dialkylamino-substituted, C_1-C_6 alkyl; and

wherein

b, c and d are the same or different, optionally halogen- or dialkylamino-substituted, C_1-C_6 alkylene; or

iii) wherein X is



wherein

a is H or, optionally halogen or dialkylamino substituted, C_1-C_6 alkyl,

and wherein

b and c are the same or different, optionally halogen- or dialkylamino-substituted, C_1-C_6 alkylene; or

iv) wherein X

is a substituted aromatic compound with three functional groupings $W_1Y_1Z_1$, wherein W, Y and Z have the meanings mentioned below;

wherein

W, Y or Z are the same or different groups CO, NH, O or S or a linker grouping capable of reacting with SH, OH, NH or NH_2;

and wherein the effector molecule E
is a cationic or anionic peptide or peptide derivative or a spermine or spermidine derivative or a glycosaminoglycane or a non-peptidic oligo/polycation or -anion; wherein
m and n are independently of each other 0, 1 or 2; wherein

p preferably is 3 to 20; and wherein

l is 1 to 5.

5. (Twice Amended) The combination according to claim 1, wherein a ligand for a higher eukaryotic cell is coupled to the copolymer.

6. (Twice Amended) The combination according to any one of claims 1-3 and 5, wherein the nucleic acid molecule is condensed with an organic polycation or cationic lipid molecule and the complex formed thereby has a charged copolymer of the general formula I bound to its surface via ionic interaction.

7. (Twice Amended) The combination according to any one of claims 1-3 and 5, containing a therapeutically effective nucleic acid molecule.

8. (Twice Amended) The combination according to any one of claims 1-3 and 5, wherein the carrier consists of a biologically non-resorbable material.

9. (Twice Amended) The combination according to any one of claims 1-3 and 5, wherein the carrier consists of a biologically resorbable material.

12. (Twice Amended) The combination according to any one of claims 1-3 and 5, wherein the carrier is a carrier which is obtainable by cross-linkage of a copolymer as defined in claim 1.

13. (Twice Amended) A method of transferring a nucleic acid molecule into a cell comprising using the combination according to any one of claims 1-3 and 5.

14. (Twice Amended) A pharmaceutical composition comprising the combination according to any one of claims 1-3 and 5.

15. (Added) The combination according to claim 1, wherein l is 1.

REMARKS

Applicants have amended the specification on page 5, lines 12-13 and claim 1 to correct an error that occurred during translation of the international application into English. Specifically, applicants have replaced "have" with "are."

Support for this amendment may be found in the specification, for example, on page 24, line 8; page 31, line 6; and page 32, line 14. Support for this amendment may also be found in the international application, for example, on page 5, lines 21-22; page 25, line 10; page 32, line 1; and page 33, line 16 of the specification and in claim 1. Applicants have enclosed copies of the relevant pages of the international application for the Examiner's convenience.

Applicants have amended claims 5-9 and 12-14 to alter their dependencies. Applicants have amended claims 1, 13 and 14 to improve their form. Support for these amendments may be found in the original claims.

Applicants have added claim 15 to recite the combination according to claim 1 wherein l is 1. Support for this amendment may be found in original claim 1.

None of these amendments add new matter. Their entry is requested.

Respectfully submitted,

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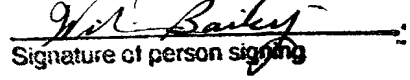
I hereby certify that this correspondence is being deposited with the U.S. Postal Service as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1327 Arlington, VA 22202, on

3/28/2002

William Bailey
Name of person signing



Signature of person signing

Version Showing Changes Made

IN THE SPECIFICATION

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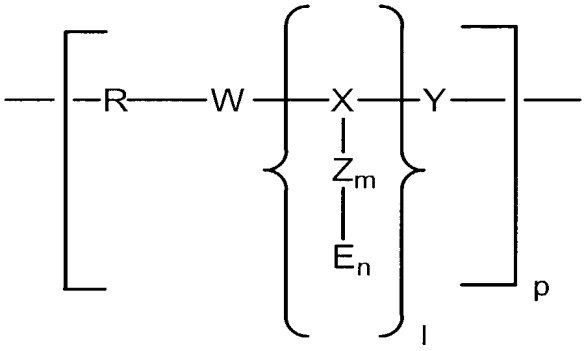

wherein R is an amphiphilic polymer or a homo- or hetero-bifunctional derivative thereof,

and wherein X

i) is an amino acid or an amino acid derivative, a peptide or a peptide derivative or a spermine or a spermidine derivative; or

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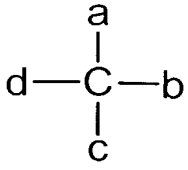

wherein

a is H or, optionally halogen- or dialkylamino-substituted, C_1-C_6 alkyl;

and wherein

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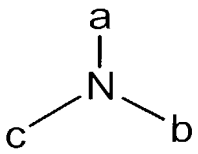

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wherein

W, Y or Z [have] <u>are</u> the same or different groups CO, NH, O or S or a linker grouping capable of reacting with SH, OH, NH or NH_2;

and wherein the effector molecule E

is a cationic or anionic peptide or peptide derivative or a spermine or spermidine derivative or a glycosaminoglycane or a non-peptidic oligo/polycation or -anion; wherein

m and n are independently of each other 0, 1 or 2; wherein

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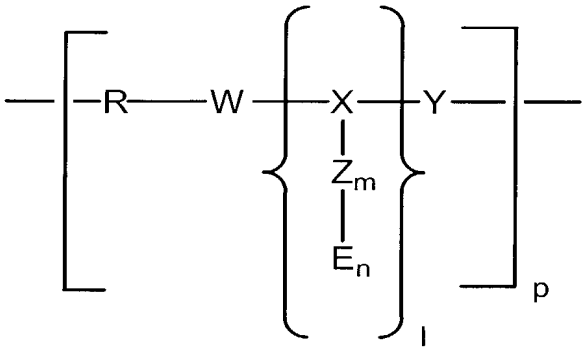

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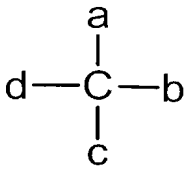

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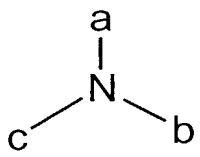

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l is 1 to 5[, preferably 1].

5. (Twice Amended) The combination according to [any one of claims 1 to 3] claim 1, wherein a ligand for a higher eukaryotic cell is coupled to the copolymer.

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13. (Twice Amended) A method of transferring a nucleic acid molecule into a cell comprising using [a] the combination according to any one of claims [1 to 3] 1-3 and 5.

14. (Twice Amended) A pharmaceutical composition comprising [a] the combination according to any one of claims [1 to 3] 1-3 and 5.